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LICATLA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053			EXAMINER SPIEGLER, ALEXANDER H	
			ART UNIT 1637	PAPER NUMBER

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary****Application No.**

10/034,934

**Applicant(s)**

RECIPON ET AL.

**Examiner**

Alexander H. Spiegler

**Art Unit**

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 September 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 6 and 10-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 7-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 41 10103
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of the Application***

1. Currently, claims 1-17 are pending. Claims 1-5 and 7-9 have been rejected and Claims 6 and 10-17 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821. This action is made NON-FINAL.

### ***Election/Restrictions***

2. Applicant's election with traverse of Group I (Claims 1-5 and 7-9, and SEQ ID NO: 8) in Applicant's response of September 2, 2003 is acknowledged.

Applicants argue the search of all the claims would be overlapping and would not cause a serious burden on the Examiner. This argument has been considered, but is not persuasive, since a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. In the instant case, the serious burden of search has been established by, at least, the different classification of the inventions (see restriction requirement and Applicant's remarks).

Applicants also argue that ten sequences should be examined. This argument has been considered, but is not persuasive, for several reasons. First, MPEP 803.04 states that "up to ten independent and distinct nucleotide sequences will be examined", which therefore, does not require that 10 sequences must always be searched. Additionally, due to the large number of sequences that have been added to sequence databases (especially since November 19, 1996 and following the sequencing of the human genome), it is a serious burden for the Office to examine more than one sequence.

Accordingly, for these reasons, and those of record, the restriction requirement is maintained.

***Specification***

3. Claims 1-5 and 7-9 objected to because the claims recite non-elected subject matter.

Applicants should amend the Claims to recite the elected sequence, SEQ ID NO: 8.

Appropriate correction is required.

***Information Disclosure Statement***

4. The information disclosure statement filed on April 10, 2003 complies with CFR 1.97, 1.98, and M.P.E.P. 609, and has been considered (see enclosed signed PTO-1449).

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-5 and 7-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 and 7-9 are indefinite over the recitation of "selectively hybridizes" because it is not clear as to what conditions permit "selective" hybridization. Applicants should amend the claims to include the specific hybridization conditions (e.g., X SSC, temperature).

***Written Description***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5 and 7-9 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1-5 and 7-9 are directed to nucleic acids that “selectively hybridize” to the nucleic acid of SEQ ID NO: 8, and nucleic acids having at least 60% sequence identity to SEQ ID NO: 8. Claims reciting 60% sequence identity and the “selective hybridization” to a nucleic acid are inclusive of sequences from other species, mutated sequences, and allelic variants having different functional activities than that of the nucleic acid (SEQ ID NO: 8) encoding the polypeptide of SEQ ID NO: 87. These claims include a large genus of nucleic acids encoding polypeptides, having unique functional activities, whereas applicants only disclose one member of the genus (i.e., SEQ ID NO: 8).

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, only one member (SEQ ID NO: 8) has been defined by its structure. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g., restriction map, chromosomal map position, biological activity of an encoded protein, etc.). In the instant case, no such identifying characteristics have been provided for any of the nucleic acids.

In *The Regents of the University of California v. Eli Lilly and Co.*, (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... 'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention".

While at the time filing Applicants were in possession of SEQ ID NO: 8, the specification does not support the broadly claimed genus. Accordingly, the claimed invention lacks an adequate written description.

#### ***Enablement***

9. Claims 1-5 and 7-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (see *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include, but are not limited to:

(1) the quantity of experimentation necessary, (2) the amount of direction or guidance

presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” *Id.* at 1404.

In the instant case, the specification does not enable one of skill in the art to make and use the claimed invention for the following reasons:

***(1) Nature of the Invention & Breadth of the Claims***

The claims are drawn to isolated nucleic acid molecules comprising SEQ ID NO: 8, a nucleic acid sequence that encodes SEQ ID NO: 87, nucleic acid sequences that “selectively hybridize” to SEQ ID NO: 8, and nucleic acid sequences have at least 60% sequence identity to SEQ ID NO: 8.

Thus, the claims are drawn to a large genus of possible nucleic acids. With respect to claim 1(c) and (d), the claims are drawn to that sequences from other species, mutated sequences, and allelic variants having different functional activities than that of the nucleic acid (SEQ ID NO: 8) encoding the polypeptide of SEQ ID NO: 87.

***(2) Relative Skill of those in the Art, State of the Prior Art, Amount of Direction or Guidance Presented & Presence or Absence of Working Examples***

The specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO: 8) were procured from, and thereby known by Incyte Genomics Inc. at the time the invention was made.

Applicants allege the nucleic acids of the present invention can be used in diagnosing lung cancer (pgs. 94-100). However, Incyte nor the specification provides the skilled artisan

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with the appropriate guidance as to how to use the claimed nucleic acids (e.g., in diagnosing lung cancer).

Applicants teach Example 1, which teaches gene expression analysis using the data mining software CLASP<sup>TM</sup> (Candidate Lead Automatic Search Program) to analyze nucleic acids from Incyte's LIFESEQ database (pg. 116-119). Specifically, Example 1 teaches CLASP<sup>TM</sup> interrogates the LIFESEQ database to identify genes that are both specific to particular tissue types as well as differentially expressed in tissues from patients with cancer, sorts the database into tissues types, categorizes each tissue sample, and then searches for genes that are expressed in the defined tissue types and differentially in the cancer disease state.

However, the specification does not teach several elements that would be necessary to enable the skilled artisan to use the nucleic acids of the invention. For example, the specification and specifically Example 1, does not teach any expression data from the analysis relating to the claimed nucleic acids (e.g., SEQ ID NO: 8). For example, the specification does not teach a comparative readout of expression among lung tissue (if tested) versus other the expression of the claimed nucleic acids in other tissues. Furthermore, the specification does not teach what sequences were being compared in the CLASP analysis, what tissues were involved, how many individuals were screened, what activity or function the polypeptide of SEQ ID NO: 87, what the statistical significance was for the CLASP 2 genes, etc.

With respect to Claim 1(c) and (d), the claims are drawn to a plurality of possible nucleotide sequence variants of SEQ ID NO: 8, wherein the specification does not provide any guidance as to how to make or alter nucleic acid sequences falling within Claim 1(c) and (d), nor does it teach how to use said sequences. Specifically, the specification is silent as to how



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nucleotide sequences falling within Claim 1(c) and (d) can be mutated and still have the function of encoding SEQ ID NO: 87, nor does the specification teach any variants of SEQ ID NO: 8. Furthermore, the specification does not teach the critical domains, if any, of the polypeptide encoded by the nucleotide sequences falling within Claim 1(c) and (d).

**(3) *Quantity of Experimentation Necessary & the Unpredictability of the Art***

Case law has established that “(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” *In re Wright* 990 F.2d 1557, 1561. In *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that “(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art”. The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art.

In the instant case, the art does not teach the association/and or correlation for any of the possible nucleic acids encompassed by the claimed invention, and thus, how to use the claimed nucleic acids in, for example, a method of diagnosing lung cancer. Since it is unclear from the teachings in the specification or the art as to how to alter the nucleotide sequences of Claim 1(c) and (d) and retain the activity of SEQ ID NO: 87, and how to use the claimed nucleic acids, absent a teaching of any expression data, or parameters for using the LIFESEQ/CLASP methodology of Example 1, it is unpredictable as to whether the claimed nucleic acids are related or associated with, or can be used in a method of diagnosing lung cancer.

In order to carry out making and using of the claimed nucleic acids, the experimentation required by the skilled artisan would be considered undue. First, the skilled artisan would have

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to experiment by altering any of the plurality of possible sequences encompassed by the claims to determine what sequences can be altered, and how they can be altered, and still retain the function of SEQ ID NO: 87. Additionally, once the sequences were obtained, the skilled artisan would have to test the expression of the sequences to determine whether the sequences are specific for diagnosing lung cancer, by carrying out expression analysis studies on many samples from different tissues from both normal and diseased test subjects. Such experimentation requires a large amount of trial and error analysis, with little to no starting point, absent any teaching in the specification (see above), wherein the results of such analysis are unpredictable, and is therefore considered undue.

In essence, the experimentation that one skilled in the art would be required to perform is in fact the proposed novelty of the invention. However, "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". (*Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001).

Accordingly, in view of the unpredictability in the art and in view of the lack of specific disclosure in the specification, undue experimentation would be required to practice the invention as it is claimed.

### ***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(f) he did not himself invent the subject matter sought to be patented.

11. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(a) as being anticipated by LIFESEQ<sup>TM</sup> Database.

The specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO: 8) were procured from, and thereby known by Incyte Genomics Inc. at the time the invention was made. Accordingly, the nucleic acids of the present invention were known and used in the art prior to the filing of the instant application.

12. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(b) based upon a public use or sale of the invention.

The specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO: 8) were procured from, and thereby known by Incyte Genomics Inc. at the time the invention was made. Accordingly, the nucleic acids of the present invention were in public use and on sale in this country prior to the filing of the instant application.

13. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO: 8) were procured from, and thereby known by Incyte Genomics Inc. at the time the invention was made. Accordingly, it appears that Applicant did not invent the claimed subject matter.

***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over LIFESEQ™ Database, in view of Prendergast (USPN 5,958,753).

As discussed in the specification (pg. 116) the nucleic acids of the present invention (including SEQ ID NO: 8) were procured from, and thereby known by Incyte Genomics Inc. at

the time the invention was made. The cited prior art does not teach expressing the nucleic acids using an expression system.

However, Prendergast teaches operably linking a polynucleotide into an expression vector, transforming a host cell with the resulting recombinant vectors and expressing the polypeptides encoded by the polynucleotide using the transformed host cells (see cols. 5-6, for example).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have linked the polynucleotides of the LIFESEQ Database into expression vectors, to have transformed host cells with the resulting vectors and to have used the transformed cells to express polypeptides in order to have provided an effective means for synthesizing polypeptides encoded by the isolated polynucleotides which would have allowed for the further characterization of the functional properties of the isolated polynucleotides and the products encoded by the isolated polynucleotides.

### ***Conclusion***

18. No claims are allowable.

### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Carla Myers, can be reached at (703) 308-2199. If attempts to reach Carla Myers are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on

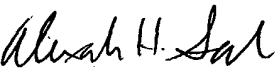
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(703) 308-1119. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
Alexander H. Spiegler  
October 16, 2003

  
CARLA J. MYERS  
PRIMARY EXAMINER